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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/769,144 | 01/30/2004 | Tibor Keler | MXI-301 | 9318 |

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| EXAMINER | |
|---|---|
| KIM, YUNSOO | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/769,144 | KELER ET AL. | |
| | Examiner | Art Unit | |
| | Yunsoo Kim | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *22-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/4/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's amendment, filed on 9/23/05 is acknowledged.
Claims 1-21 have been canceled.
Claims 22 and 32 have been amended.
Claims 22-49 are pending.

2. Applicant's election without traverse of Group II in the reply filed on 9/23/05 is acknowledged. Claims 22-49 are under consideration in the instant application.

3. Sequence compliance: The instant application appears to be in sequence compliance for patent application containing nucleotide sequence and/or amino acid sequence disclosures.

4. Applicant's claim for domestic priority under 35.U.S.C.119 (e) is acknowledged.

5. Applicant's IDS filed on 2/4/05 is acknowledged.

6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (p. 14, lines 10 and 18). Applicant is required to delete the embedded hyperlink and/or other form of browser executable code. See MPEP 608.01 and 608.01(p).

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 41-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody that binds to an antigen presenting cell (APC) wherein the antibody consisting of human heavy chain variable region comprising of FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4 and a human light chain variable region comprising FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4 or any human heavy chain or light chain variable region consisting of SEQ ID NO: 4 and 8, or CDRs identified as in SEQ ID NOs: 13-18, does not reasonably provide enablement for any antibody comprising "conservative modifications thereof" or "substantially homologous to" the SEQ ID NOs disclosed in claims 41-44).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Given the established unpredictability of the art, the instant specification would require a significant guidance to how to make and use "conservative modification" and " sufficiently homologous" to SEQ ID NOs: 4, 8, 13-18. It is unlikely that the generic modified molecular conjugates encompassed by the claims would function for their intended use. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al. (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function.

Applicant has no working examples demonstrating any modified molecular conjugates or sufficiently homologous antibody to antigen presenting cell (APC).

To summarize, reasonable correlation must exist between the scope or the claims and scope of the enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breath of the claims, it would take undue trials and errors to practice the claimed invention.

9. Claims 41-44 are rejected under 35.U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an antibody that binds to an antigen presenting cell (APC) wherein the antibody consisting of human heavy chain variable region comprising of FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4 and a human light chain variable region comprising FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4 or any human heavy chain or light chain variable region consisting of SEQ ID NO: 4 and 8, or CDRs identified as in SEQ ID NOs: 13-18, however, applicant is not in possession of any antibody comprising "conservative modifications thereof" or "substantially homologous to" the SEQ ID NOs disclosed in claims 41-44.

There is insufficient written description encompassing "conservative modifications thereof" or "substantially homologous to" SEQ ID NOs: 4, 8, 13-18 as recited in claims 41-44 because any amino acid sequence of different chemical or physical properties of amino acid is not set forth in the specification as filed, commensurate in scope with the claimed invention. Therefore, Applicant does not possess the scope of claimed invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use.

Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601,1606 (CAFC 1993).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 33-45 and 47-49 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO 01/85798 A2 (IDS reference).

The '798 publication teaches an human monoclonal antibody to antigen presenting cell (i.e. dendritic cells) conjugated to tumor antigen (p. 5-6, 54-55), in vivo and ex vivo internalization of antigen by APC, immune response mediated by MHC-I/II complexes, antibody being Fab and use of immunostimulatory cytokines as adjuvant (i.e. GM-CSF, p. 57) (p. 5-6, 26, 38-41, 56-58, claims 16, 23-27, 32, 38-42).

The '798 publication further teaches the antibody mediates cytotoxic T cell response (p. 6, 35-36) and antibody comprising SEQ ID NOs: 4 and 8 (example 2, SEQ ID NOs: 2 and 4). As the SEQ ID NOs: 4 and 8 encompass the CDRs identified as in SEQ ID NOs: 13-18, the reference teaching meets the claimed limitation.

Claims 37 and 38 are included in this rejection because as evidenced by the specification of the instant application p. 14, lines 14-18, the antibody encompasses the B11, and the referenced antibody teaches B11 (referenced SEQ ID NOs: 2 and 4), binding to a C type lectin on the dendritic cells and human mannose receptor is the inherent property of the of the anti-APC antibody.

Therefore, reference teachings anticipate the claimed invention.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 22-33 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/85798 (IDS reference) in view of U.S. Pat. No. 5,869,057 (IDS reference).

The teachings of the '798 publication have been discussed, supra.

The '798 publication does not teach the use of βhCG as an antigen.

However, the '057 patent teaches the use of βhCG as an antigen (i.e. detectable on the 74 cancer cell lines, col. 3, lines 40-50, col. 5, lines 32-60). The '057 patent further teaches the βhCG general tumor antigen which could be using immunization against βhCG as an antimetastasis treatment.

Therefore, one of the ordinary skill in the art would have been motivated to combine the teachings of the '057 patent into the molecular conjugate binds to dendritic cells and tumor antigen taught by the '798 publication because of the availability and well known characteristics of of βhCG as tumor antigen.

From the teachings of references, it would have been obvious to one of the ordinary skill in art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary skill in the art at the time of invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 22, 32 and 33 are provisionally rejected under the judicially created doctrine of double patenting over pending claims 39-44 of copending Application No. 10/903,191. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.
Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims encompass a method of inducing T cell mediated response comprising and antibody to APC and βhCG as tumor antigen.

16. No claims are allowable.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yunsoo Kim whose telephone number is 571-272-3176. The examiner can normally be reached on Monday thru Friday 8:30 - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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December 12, 2005

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